



**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

11

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/431,469	11/01/99	ARMISTEAD	D VPI/95-09-DI

JAMES F HALEY JR
FISH & NEAVE
1251 AVENUE OF THE AMERICAS
NEW YORK NY 10020-1104

HM12/0104

EXAMINER

MORAN, M

ART UNIT

PAPER NUMBER

1631

DATE MAILED:

8
01/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/431,469

Applicant(s)

ARMISTEAD ET AL.

Examiner

Marjorie Moran

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-24 is/are rejected.
- 7) ☒ Claim(s) 19-22 and 24 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group III, claim 13 in Paper No. 6, filed 10/10/00 is acknowledged. Claim 13 has been canceled and new claims 19-24 added. Applicant states in the repines filed 10/10/00 that claim 19-24 read on elected Group III, therefore claims 19-24 are also considered elected.

An action on the merits of elected claims 19-24 follows.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Claim Objections

Claims 19-22 and 24 are objected to because of the following informalities: Each of claims 19-22 and 24 recites the term "CnA". Similarly, claims 21 and 24 recite the term "CnB". Although the terms are defined by the specification on page 2, the full terms are not recited in the claims. For clarity, the examiner recommends that the full terms, --calcineurin A--, and --calcineurin B--, be recited at least once in the claims.

Art Unit: 1631

Although the terms "FKBP12" and "FK506" are also abbreviations, the most commonly used terms for these compounds in the art are "FKBP12" and "FK506", therefore the limitations intended by these terms are considered sufficiently clear. Claim 21 recites the term "123" twice in line 7. As structure coordinates are usually distinct, the examiner interprets this to be a typographical error. Appropriate correction is required. For purposes of applying the prior art, claim 21 will be treated as if it recited --122, 123, 124, 157 ...-- in line 7.

Claim Rejections - 35 USC § 112

Examiner's note: Each of claims 19-20 and 22-23 recites the phrase "according to Figure 1". Incorporation by reference to a figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than by duplicating a drawing or table into the claim". MPEP 2173.05(s). In the case of the instant claims, there is no practical way to express the atomic coordinates of Table 1 in words, and Table 1 is so large that it would be impractical to reproduce it in the claims, therefore the incorporation by reference of Table 1 is considered a proper claim limitation, and is not indefinite. Applicant should note that changes to Table 1 may be considered a new claim limitation and may result in new matter rejections.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1631

Claims 19-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19-23 recite the term "homologue". The term is not defined by the specification or claims and may have several meanings in the art; e.g. structurally similar, physiologically similar, of similar activity, etc. It is noted that a structural homologue does not necessarily display similar activity, while compounds with similar activities are not necessarily structurally similar. As it is unclear what meaning applicant intends for the term "homologue", its use renders the claims indefinite.

Claims 19 and 21 recite the term "a binding pocket", each in step (a). It is unclear whether the binding pocket of step (a) is intended to be the same as the binding pocket defined by the structure coordinates of lines 3-6 of claim 19 and lines 3-8 of claim 21, is intended to be the same as the binding pocket of lines 8-10 of claim 19 and lines 10-12 of claim 21, or a different binding pocket than either of those recited earlier in the claims, therefore the claims are indefinite.

Claims 19 and 21 recite "the binding pocket", each in step (b). The antecedent basis for this term is unclear (i.e. the binding pocket defined by structure coordinates (lines 3-6 or 3-8, respectively), the binding pocket of lines 8-10 or 10-12, respectively, or the binding pocket of step (a)), therefore each claim is indefinite.

Claim 20 recites the term "said binding pocket" with regard to claim 19. Claim 19 recites several binding pockets, therefore the antecedent basis for "said binding pocket" is unclear, and claim 20 is indefinite.

Claim 21 recites the term "said amino acids" in line 11. It is unclear whether the antecedent basis for this term is CnA amino acids, CnB amino acids, or both, therefore the claim is indefinite.

Claim 22 further limits the crystallized molecule or molecular complex of claim 21 to comprise a "second binding pocket" defined by certain structure coordinates. The limitation of a "second binding pocket" is further limiting for claim 21, therefore claim 22 is properly dependent on claim 21. However, the CnA structure coordinates recited in claim 22 are identical to those recited for the CnA coordinates for the (first) binding pocket of claim 21, therefore it is unclear what the structure coordinates of claim 22 are intended to represent. In addition, it is unclear what metes and bounds are intended by applicant for a "second binding pocket". For these reasons, claim 22 is indefinite. The examiner interprets a "second" binding pocket to be different from the (first) binding pocket of claim 21. However, as it is unclear what structure coordinates correspond to a "second" binding pocket, claim 21 is interpreted to recite only a second binding pocket, without any limitations with regard to structure coordinates.

Claim 23 recites "the set of structure coordinates" in lines 2-3. The antecedent basis for this phrase is unclear. Claim 23 is dependent on claim 22 which recites amino acids. Claim 22 is dependent on claim 21, which defines amino acids as "structure coordinates", thereby supplying an antecedent basis for "structure coordinates". However, claim 21 also recites two different "sets" of structure coordinates, therefore it is unclear which "set" of structure coordinates is intended to be the antecedent basis for the phrase "the set of structure coordinates". In addition, it is

unclear what constitutes a "set" of structure coordinates (i.e. CnA amino acids only; CnB amino acids only, a totality of CnA and CnB, or some other group of coordinates). For these reasons, claim 23 is indefinite.

Claim 23 recites the term "said amino acids" in line 5. The antecedent basis for this term is unclear, therefore the claim is indefinite.

Claim 24 limits the molecule or molecular complex to comprise amino acids 17-392 of four different compounds. It is unclear what limitation is intended; i.e. amino acids 17-392 of each compound; 17-392 of a single compound, 17-392 of a complex wherein amino acids are numbered differently from those in any single protein; 17-392 of some fusion protein comprising amino acids from all four named compounds, etc., therefore the claim is indefinite.

Claim 24 is indefinite because it is not commensurate in scope with the teachings of the specification. Claim 24 recites a molecule or molecular complex comprising amino acids 17-392 of CnA, CnB, FKBP12, and FK506. The specification provides support on page 12 for a complex which comprises amino acids 17-392 of CnA, and amino acids 5-169 of CnB. The specification provides further support on page 35 for a model of a complex comprising residues 24-240 and 247-370 of CnA, residues 5-82 and 84-168 of CnB, and residues 1-107 of FKBP12. Nowhere does the specification teach a molecule or molecular complex comprising amino acids (or residues) 17-392 of a combination of CnA, CnB, FKBP12, and FK506. Nor does the specification provide support for a molecule or complex comprising amino acids 17-392 of each of the recited compounds. The specification does not provide support for the scope of claim 24,

Art Unit: 1631

therefore it is unclear what limitation is intended and the claim is indefinite. It is noted that if applicant intends a complex comprising CnB, FK506, FKBP12, and amino acids 17-392 of CnA, the claim is still indefinite as the specification does not support a complex of FKBP12, FK506, and the full length of CnB with particular amino acids of CnA. See above.

Conclusion

Claims 19-24 are rejected but appear to be free of the prior art.

The prior art made of record and not relied upon which is considered pertinent to applicant's disclosure is MILAN et al. (Cell, 79, pages 437-447, 11/1994), who teaches molecular modeling of CnB. MILAN also teaches modeling of CnB interactions with a truncated CnA, but does not teach modeling of binding or active sites on CnA. The prior art of ANGLISTER et al. (Biochemistry, 33, pages 3540-3547, 1994) also teaches three-dimensional modeling of CnB and structural coordinates for amino acids therein (see Figure 1), but does not teach 3D modeling of CnA. The prior art of CHENG et al. (Biochemistry, 33, pages 4093-4100, 1994) teaches that an FKBP12/FK506 complex has been well characterized by X-ray crystallography and NMR, and teaches that the complex binds to (associates with) calcineurin (page 4094). While CHENG suggests that the interface between the binary complex and calcineurin be characterized (page 3094, first full paragraph), he also teaches that there is no 3D structural information known for the ternary complex. CHANG does not teach 3D modeling of a binding pocket on CnA. The prior art of BARFORD et al. (J. Molec. Biol., 235, pages 763-766,

Art Unit: 1631


1994) teaches crystallization of protein phosphatase 1 (PP1). However, although PP1 is an enzyme related to calcineurin (protein phosphatase 2B, or PP2B), the two enzymes bind different inhibitors (see page 763), therefore they would not necessarily be expected to comprise the same structure coordinates for their binding pockets.

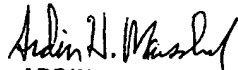
KISSINGER et al. (Nature, 378, pages 641-644, 12/1995) and GRIFFITH et al. (Cell, 82, pages 507-522, 8/11/1995) teach crystal (X-ray) structures of calcineurin (CnA and CnB) and complexes with inhibitors; however, neither is prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524.


Marjorie A. Moran
December 28, 2000


ARDIN H. MARSCHEL
PRIMARY EXAMINER